**PHP163**
**PHARMACEUTICAL INNOVATION: DEFINITION, AND MECHANISMS FOR REWARD**
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**OBJECTIVES:** To define the concept of pharmaceutical innovation, examine whether it merits reward, and identify mechanisms for its incentivisation. **METHODS:** Whether or not a medicine is innovative dependents on its novelty and the benefits it generates. Novelty requires something new, original and perhaps ingenious and is a necessary, but not sufficient, requirement for innovation. Novel pharmaceutical attributes include: new target of pharmacological mechanism of action, new chemical structure, improved formulation, improved pharmacokinetics and efficient methods of production. Benefits depend on perspective. Whereas a patient would value health-related quality of life, life expectancy, safety and convenience, payers of healthcare (e.g. UK NHS) may legitimately value population health and cost-effectiveness. A society might additionally value non-health benefits such as attracting pharmaceutical company investment in skilled jobs, and social responsibility (e.g. environment, neglected diseases). **RESULTS:** An effective vaccine developed in the UK against malaria would be considered highly innovative from a societal perspective, but not from an NHS perspective, as malaria does not affect NHS patients. CONCLUSION: Health benefits to NHS patients are already rewarded to (and in some cases beyond) the threshold for cost-effectiveness (£30,000 per QALY). There is no incentive for paying an additional premium. However, where benefits of innovation to society exceed the costs, there is an argument for reward. This should not be through price increases, but through taxation and patent laws. The Patent Box, which will decrease the corporation tax to 10% on profits from UK patents, is one such mechanism. Alternatively, a 'value-based patenting' scheme might vary patent duration according to the benefits achieved, as the clinical evidence matures from the time of licensing. This might benefit patients through the earlier introduction of generics when branded products are mediocre, reward genuinely innovative products, while still allowing the introduction of 'me-toos' to compete on price.

**PHP164**
**A TYPOLOGY OF OUTCOMES FOR HEALTH RESEARCH**
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Measuring "outcomes" is at the heart of this Society's mission and of efforts to improve health and health care delivery. Despite this central role, there is no common agreed-upon definition as to what is meant by outcomes. For example, for some commentators, outcomes refer uniquely to quality-of-life and survival of individual patients; this thinking underlies the US Patient Centered Outcomes Research Institute. For others, including those doing economic evaluation, outcomes may refer to the average health benefit groups of patients. Yet others use "outcomes" to refer to aspects of functioning of the health care system. This lack of consistency does little to illuminate the challenges in equitably delivering timely, high quality, and affordable health care. In this presentation, the authors present a typology of outcomes for health research along with and relevant examples. At the most granular level, endpoints in randomized trials are often clinical outcomes which are characterized as immediately observable - "hard" - such as hospitalization, death or functional status, or latent - "soft" - such as quality-of-life, pain, or satisfaction. At the next level are health outcomes which are the results of care delivered in actual practice and can be subdivided into: treatment outcomes which reflect the intended and unintended medical consequences of undergoing therapy and patient outcomes which reflect the impact on patients of undergoing care in the real world. System outcomes can be thought of as the impact of delivering care to a group of patients and are measures of the degree of functionality of the health care system. At the highest level are societal outcomes, which measure the impact of health on the wellbeing of society. Consensus as to what is meant by "outcomes" would be an important step towards improving the quality of the discourse and critical thinking in this area.

**PHP165**
**A NEW ANTI-REBATE LEGISLATION IN SOUTH KOREA: WILL IT WORK THIS TIME?**
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**OBJECTIVES:** The objective of this study is to examine the potential impact of recent reform in anti-rebate law of drugs in South Korea. **METHODS:** It has been an old business practice that some doctors and pharmacists receive financial benefits from pharmaceutical companies and distributors in exchange for business favors in Korea. These kickbacks are considered 'unethical and illegal drug rebates'. The Korea Fair Trade Commission reckoned consumer damage caused by illegal rebates in the medicines market at about US$2.02 billion, accounting for about 20% of total pharmaceutical sales in the year of 2007. There are a couple of reasons why illegal drug rebate is so prevalent in Korea. First, the current drug pricing system guarantees relatively good prices for generic products which local companies focus on producing. Good prices tend to leave rooms for marketing and illegal rebates. On top of that, there are lots of small scale suppliers relative to the pharmaceutical market size of Korea. Fierce competitions among drug suppliers make them concentrate on marketing activities, often coupled with illegal rebates. Third, government has no control over the visits by drug company representatives to doctors' offices. In addition, almost no medical treatment guidelines which could effectively regulate doctor's prescription behavior exist. **RESULTS:** Previously, any illegal marketing practice by drug companies led to criminal punishment of drug companies alone, leaving doctors and pharmacists untouched. Under the new legislation, punishment for illegal rebate is now extended to doctors and pharmacists. By penalizing both rebate givers and receivers, it is hoped that the level of illegal rebate can be disappeared or substantially reduced from the Korean market. However, we need to see what might happen in the real market practices from now on. **CONCLUSIONS:** Remaining issues with this anti-rebate reform will be explored in this study.

**PHP166**
**ON-GOING MARKET ACCESS ADVICE A POSSIBLE SOLUTION TO HELP ENSURE LONG-TERM SUCCESS IN POST-MARKETING CLINICAL STUDIES: CROSS FUNCTIONAL TEAMS OR EXTERNAL CONSULTATION?**
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**OBJECTIVES:** Manufacturers are under increasing pressure to conduct shorter clinical trials in order to bring products to market as soon as possible and ensure revenue maximisation before loss of exclusivity. At the same time, authorities from markets across the globe have demonstrated increased interest in post-marketing real-life clinical data in order to help make decisions with regards to reimbursement of drugs as well as their positioning in the treatment pathway. **METHODS:** Manufacturers are spending increasing proportion of their budgets to produce this post-marketing clinical data. It is important to ensure if the data that is being produced is close to the needs of the payers. In majority of instances, it is seen that the data being created is quite far from the expectations of authorities to whose benefit it is being created. The data is typically considered for use in payer discussions only at the end of the clinical study when little flexibility is possible in the end-points and outcomes that will be demonstrated. Also, benefits such as considering early data cuts to present on-going benefit of this long term data is not usually seen. **RESULTS:** ; Market access, outcomes research and medical affairs teams tend to function independently with very little collaboration as a result of differing targets and budgets. This has made it difficult to have early payer-focussed input into clinical studies. This is particularly so if they are post-marketing studies involving teams with lower focus on payer needs compared to peri-launch market access teams. There is an increased need for greater cross-functional effort on producing clinical data to ensure efficient use. **CONCLUSIONS:** Involving an external market access agency that is able to advise on the production, analysis and use of post-marketing clinical data is seen to be the solution to this issue.

**PHP167**
**TELL ME WHO YOUR FRIENDS ARE: "PEERS" IN COMPARING HEALTH CARE SYSTEMS**
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Total health spending and its share in the social product have been staple indicators in assessing and comparing health care systems. Comparison of health care systems based on Euros and cents is limiting, however, since the health care system is not an artifact of the economy. Institutions shape societal values on health care leading to peculiarities even among health care systems that share traditions in terms of health care financing and delivery. This paper presents a framework to compare health care systems in a meaningful way that accounts for systemic differences and similarities using the empirical technique cluster analysis. The analysis will follow a three-step procedure. A review of the literature will be conducted to identify major institutional indicators of any given health care system. Cluster analysis will then be employed using these indicators based on data of OECD member countries. Based on the isolated clusters using the "minimum description length" approach, "peer" health care systems will be identified and described highlighting so-called leaders of the pack. At the heart of the performance of every health care system is the extent to which it is able to respond to the desire for a healthy life by members of society. This implies accounting for both efficiency, which investigates the link between the link between health care resources and health outcomes, and effectiveness, which assesses the achievement of goals rather than choosing one over the other. Assessing health care systems against peers and over time would not only set systems apart given their shared intent of ensuring health by providing health care but may well engender learning and lead to a race to the top.

**PHP168**
**ENDOGENOUS COST-EFFECTIVENESS ANALYSIS IN HEALTH CARE TECHNOLOGY ADOPTION**
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Increased health care spending across developed nations, including the US, has put pressure on both public and private payers. The current literature has attributed this growth in spending as being largely due to technological change. To prioritize adoption of new technologies, so called cost-effectiveness analysis has been used as the main tool by third-party payers and, as a result, has generated perhaps the largest sub-field within health economics. In this paper we argue utilization of cost-effectiveness analysis is subject to a form of Lucas critique; the stated goals of the policy will not materialize when those affected by it respond to it. In particular, we stress that cost-effectiveness analysis by payers invariably reflects prices set by producers rather than resource costs used to produce treatments. This implies that the "costs" in cost-effectiveness assessments depend on endogenous markups which are, in turn, influenced by demand factors of patients, doctors, and, most importantly, the cost-effectiveness policy used by payers to translate prices to adoption decisions. We argue this has two important implications. First, under

endogenous cost-effectiveness analysis policies aimed at lowering spending may actually raise it. Second, reimbursement policy based on endogenous cost-effectiveness levels may lead to adoption of more inefficient treatments. Under the standard conditions when producer costs are unobservable, we provide a test for these conditions using data on technology appraisals in the UK 1999-2005.

PHP169

### THE VALUES OF GENERAL PRACTITIONERS/FAMILY PHYSICIANS SHOULD BE FOSTERED INTO OTHER CLINICIANS: A RESEARCH STUDY

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**OBJECTIVES:** The paper is to improve the quality of life and health of the peoples of the world by fostering and maintaining high standards of care in general practice/family medicine and other clinicians. **METHODS:** By comparing the general practitioners/family physicians with the clinicians of specialities, summarizing the shortcomings of present health care services, the proposals for promoting health care services around the world were suggested. **RESULTS:** The article initiates that the values of general practice/family medicine should be fostered into other clinicians when all the clinicians take care of the patients in any conditions, critical or ordinary, by adopting to the values of general practice/family medicine. While the clinicians also take into account of their own specialities. **CONCLUSIONS:** In applying these proposals, a healthy world and high quality of life of the peoples of the world will come soon! So the quality of life and health of the peoples of the world can be promoted and enhanced.

## Cardiovascular Disorders – Clinical Outcomes Studies

PCV1

### EXPLORATIVE ANALYSIS ABOUT THE APPROPRIATENESS OF A GPS LONGITUDINAL DATABASE ON EVALUATING ATYPICAL ANTIPSYCHOTICS IN TERMS OF DRUGS ADVERSE EVENTS

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**OBJECTIVES:** The main objective of this study was to understand the appropriateness of a GPs Longitudinal Database on exploring potential causal associations among therapies and adverse events. We've focused on subjects treated with three of the most widespread atypical antipsychotics drugs known as affecting patients' lipidic profile and cardiovascular and diabetes risk. **METHODS:** Data were obtained from CSD LPD, an Italian General Practitioner's longitudinal database. Patients with a first prescriptions of Aripiprazole, Olanzapine or Quetiapine during the period January 2005 to December 2009 have been selected. For each patient, the first prescription has been considered as the Index Date. The final study sample was composed of patients that during the following three months had at least another prescription of the same atypical antipsychotic. Patients have been followed-up for a maximum of 12 months starting from three months after the Index Date. **RESULTS:** Treatment groups were composed of 367 patients for Aripiprazole, 1825 patients for Olanzapine and 3088 patients for Quetiapine. The proportion of patients with an out of range value of Total Cholesterol and LDL was significantly lower in Aripiprazole group. The same trend has been observed for the proportion of patients with at least one recorded diagnosis of cardiovascular events and diabetes. The association between treatment and cardiovascular diagnosis presence was still significant even when performing a multivariate logistic model adjusted for age, gender and presence of a cardiovascular diagnosis during the year before the Index Date (Odds Ratio Olanzapine VS. Aripiprazole: 1.76 [1.08 – 2.85]; Odds Ratio Quetiapine versus Aripiprazole: 1.67 [1.03 – 2.70]). **CONCLUSIONS:** CSD LPD database resulted to be appropriate in exploring potential causal associations among treatments and potential adverse events both in terms of recorded diagnosis and in terms of recorded laboratory exams values even if, in this case, the sample size was reduced.

PCV2

### EVALUATION OF THE PROPHYLAXIS PATTERNS AND 90 DAY OUTCOME EVENTS IN HOSPITALIZED MEDICALLY ILL PATIENTS

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**OBJECTIVES:** To compare the prophylaxis patterns, incidence of venous thromboembolism (VTE), major and minor bleeding and readmission over 90 days in hospitalized medically ill patients. **METHODS:** A retrospective study (January 1, 2005 to December 31, 2007) was conducted using a health insurance claims database. Eligible patients were selected if they were continuously enrolled in their health plan for at least 180 days prior to and 90 days following the index hospital discharge, for which they were hospitalized with a medically ill diagnosis. Prophylaxis use was defined as receiving low molecular weight heparin (LMWH) only, warfarin only, unfractionated heparin (UFH) only, fondaparinux only, LMWH and warfarin, or UFH and warfarin, from the index hospitalization date to 30 days after index hospital discharge and before VTE events. Risk-adjusted venous thromboembolism and major and minor bleeding events among patients with different thromboprophylaxis patterns were compared. **RESULTS:** In patients who were identified as medically ill (n=12,077), 6,464 (53.52%) received anticoagulant therapy during their hospitalization and until 30 days after discharge. Among these patients who received prophylaxis, 2,137 (33.06%) received LMWH only, 693 (10.72%) received warfarin only, 2168 (33.54%) received UFH only, 12 (0.19%) received fondaparinux only, 291 (4.50%) received LMWH and warfarin, and 325 (5.03%) received UFH and warfarin. Among the 6 prophylaxis patterns, patients who received LMWH only were associated with lower VTE (0.39% vs. 1.98%, p=0.0001) and readmission rates (8.38% vs. 13.68%, p=0.0049) than those with LMWH and warfarin combination therapy. In addition, the LMWH only group of patients had lower rates of major and minor bleeding than the UFH and warfarin combination therapy group. **CONCLUSIONS:** Despite existing guidelines, few medically ill patients receive anticoagulant prophylaxis. Appropriate anticoagulant prophylaxis results in lower VTE event rates in hospitalized medically ill patients.

PCV3

### THROMBOPROPHYLAXIS USE AND VENOUS THROMBOEMBOLISM, MAJOR AND MINOR BLEEDING EVENT ANALYSIS IN HOSPITALIZED MEDICALLY ILL PATIENTS

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**OBJECTIVES:** To assess the real-world rate of appropriate prophylaxis use for incidences of venous thromboembolism (VTE), and major and minor bleeding in hospitalized medically ill patients. **METHODS:** A retrospective study (January 01, 2005 to December 31, 2007) was conducted using a health insurance claims database. Eligible patients were selected if they were continuously enrolled in their health plan for at least 180 days prior to and 30 days following the index hospital discharge date, for which they were hospitalized with a medically ill diagnosis. Prophylaxis use was defined as receiving low molecular weight heparin (LMWH) only, warfarin only, unfractionated heparin (UFH) only, fondaparinux only, LMWH and warfarin, or UFH and warfarin, from the index hospitalization admission date to 30 days after index hospital discharge, and before VTE events. Risk-adjusted VTE and major and minor bleeding events among patients with different thromboprophylaxis patterns were compared. **RESULTS:** In patients who were identified as medically ill (n=12,947), 6,949 (53.67%) received anticoagulant therapy during their hospitalization and until 30 days after discharge. Among those patients who received prophylaxis, 2,295 (33.03%) received LMWH only, 752 (10.82%) received warfarin only, 2,313 (33.29%) received UFH only, 12 (0.17%) received fondaparinux only, 309 (4.45%) received LMWH and warfarin, and 353 (5.08%) received UFH and warfarin. Compared with patients who received LMWH only, patients who received the combination therapy of LMWH and warfarin had significantly more VTE events (1.14% vs. 0.32%, p=0.0099) and higher readmission rates (6.11% vs. 3.05%, p=0.0093), while patients who received the combination therapy of UFH and warfarin had significantly higher minor bleeding (11.70% vs. 6.06%, p=0.0002) and readmission rates (7.49% vs. 3.05%, p=0.0001). **CONCLUSIONS:** Appropriate anticoagulant prophylaxis use results in lower VTE event rates as well as lower major and minor bleeding rates in hospitalized medically ill patients. More effort is required to improve the use of appropriate thromboprophylaxis.

PCV4

### COMPARATIVE EFFICACY OF MAINTENANCE OF SINUS RHYTHM VERSUS RATE CONTROL STRATEGIES IN THE TREATMENT OF ATRIAL FIBRILLATION – SYSTEMATIC REVIEW AND META-ANALYSES

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**OBJECTIVES:** The aim of this study was to assess whether restoration and maintenance of sinus rhythm is associated with clinically meaningful improvement in patients with atrial fibrillation (AF) or atrial flutter (AFI). **METHODS:** Assessment was based on randomized controlled trials (RCTs) identified by means of systematic review, carried out according to the Cochrane Collaboration guidelines. Studies met the inclusion criteria if they directly compared two treatment strategies, i.e. maintenance of sinus rhythm (MSR) including first generation antiarrhythmic drugs (FGAAD; mainly amiodarone, sotalol, dizopiramide, propafenone, dofetilide, flecainide) vs. rate control (RC) including pharmacologic agents (calcium channel blockers, beta blockers, cardiac glycosides), with regard to clinically meaningful endpoints. The most important medical databases (EMBASE, MEDLINE and CENTRAL) were searched until January 2011. Two reviewers independently selected trials, assessed their quality and extracted data. **RESULTS:** Eight RCTs directly comparing MSR vs RC were identified and included. Meta-analysis of those studies showed that significantly more patients assigned to MSR were in sinus rhythm at the end of study as compared to RC strategy (RB = 4.49 [2.49; 8.09]; NNT13-37months = 2 [2-4]). However, it did not lead to any benefit regarding clinically meaningful endpoints. Comparison between both treatment strategies revealed no statistically significant difference with respect to risk of overall mortality (RR = 1.06 [0.96; 1.17]), cardiovascular mortality (RR = 1.01 [0.88; 1.16]), stroke (RR = 1.02 [0.82; 1.26]), systemic embolism (RR = 0.78 [0.35; 1.71]), heart failure (RR = 0.94 [0.80; 1.09]) or bleeding (RR = 1.10 [0.65; 1.84]). **CONCLUSIONS:** In this analysis, restoration and maintenance of sinus rhythm achieved with FGAAD was not associated with clinically meaningful improvement in patients with AF or AFl. MSR strategy neither improved survival nor decreased morbidity as compared to RC. The reevaluation of current criteria of antiarrhythmic drug assessment should be considered.

PCV5

### THROMBOEMBOLISMS WITH THROMBOPOIETIN RECEPTOR AGONISTS: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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